

EXHIBIT A

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PATENT APPLICATION

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:	)	
	:	Examiner: P.K. Sripada
HARALD BREIVIK, et al.	)	
	:	Group Art Unit: 1202
Serial No.: 07/902,500	)	
	:	Attorney Docket No.
Filed: June 23, 1992	)	1526.100 Cont. I
	:	
For: FATTY ACID COMPOSITION	)	

The Honorable Commissioner of Patents  
and Trademarks  
Washington, D.C. 20231

RULE 132 DECLARATION BY JEANNE D. JOSEPH

I, Jeanne D. Joseph, a resident of Charleston,  
South Carolina, do hereby declare as follows:

1) Qualifications:

I am a research chemist, recently retired from the National Marine Fisheries Service, where I worked for 16 years, at the Service's Charleston Laboratory. The National Marine Fisheries Service is within the U.S. Department of Commerce, under the National Oceanic and Atmospheric Administration. My specialty is lipid chemistry, a field in which I have worked since 1969. I have a B.S. in Physiology from Florida State University, awarded in 1952, and I have done graduate work in physiology, biochemistry, and biophysics at Florida State University and Tulane University.

Attached as Exhibit A is a copy of my curriculum vita, which accurately reports my scientific education, training, and experience.

2) Familiarity With Cornieri et al.  
and Breivik Declaration:

I have carefully read and considered U.S. Patent No. 5,130,061 to Cornieri et al., a copy of which is attached as Exhibit B, as well as the August 12, 1994 Declaration by Dr. Harald Breivik, a copy of which is attached as Exhibit C. The work with fish oil products that is reported in these documents is akin to work I did at the National Marine Fisheries Service, and which is within my field of expertise.

3) Purpose of Review:

I was asked to review and evaluate the studies reported by Dr. Breivik in his Declaration, and to render an opinion on the following questions:

a) Given his stated objectives (page 2, lines 6-11), was the procedure Dr. Breivik followed (as reported in his Declaration) in his attempt to replicate the examples in Cornieri et al. logical and correct?

b) Were the results credible?

c) Are Dr. Breivik's conclusions (page 10, paragraph 3) reasonable?

4) Conclusions:

In my expert opinion:

a) The procedure Dr. Breivik reported using was logical and correct.

b) The results Dr. Breivik reported obtaining are credible.

c) The conclusions Dr. Breivik reached are reasonable.

5) Additional Observations:

Given Dr. Breivik's stated objectives, I do believe that the research was both logical and correct. His purpose, basically, was to reproduce the results cited in the Cornieri patent and to determine the EPA:DHA ratios in the various products yielded. The Cornieri patent does not state what still capacity, residence time, or feed rate was used. Nevertheless, as shown by Dr. Breivik's data tables, he endeavored to determine optimal temperatures and feed rates to achieve the desired end results.

His results were credible and, in fact, provided far more detail in the composition of the products - not just area percentages of EPA and DHA, but also weight percentages of these compounds, and in addition, yields of distillate and residue (also in weight percent).

The conclusions drawn from this research are both reasonable and valid, based upon the numerical data submitted.

Attached as Exhibit D is a table I created for two purposes. The first was to demonstrate numerically that area percentages and weight percentages are two different entities altogether, which is evident from close scrutiny of Dr. Breivik's five tables. Secondly, calculation of the A%:Wt.% ratios for EPA, DHA, and EPA+DHA allowed me to determine a "correction factor" of approximately 1.5:1. If

this correction factor is applied to the (presumed) area percentages cited in the Cornieri patent, the weight percentage of the Example 10 product, for instance, is approximately 65%, rather than the stated 96%. If one uses the range of correction factors for DHA alone (1.81 - 1.27) the possible composition of the product of Example 10 can be anywhere between 53.0 and 75.6 weight percent. These same A%:Wt% calculations could also be carried out on the collaborative study data published in Joseph, J.D., & Ackman, R.G. (1992) *J. Assoc. Off. Anal. Chem.* 75, 488-506 (copy attached as Exhibit E). A quick spot check shows somewhat lower correction factors -- about 1.1 to 1.3.

It is clear from the published scientific literature, <sup>2/</sup> that content of fish oil fatty acids in medicinal products can only be validly expressed as weight percent of the composition, or in a similar unit such as mg/gram of sample or dose. As Dr. Breivik indicates in his Declaration, area percent composition is a quick and easy GLC check on the progress of an ongoing process, but the definition of the absolute composition of the product, i.e. the weight percent composition, is required by the European

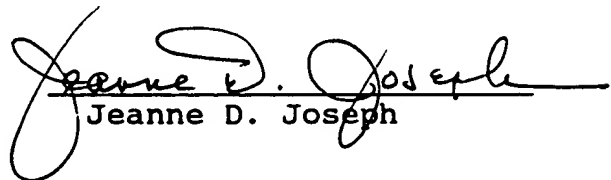
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<sup>2/</sup> Jeanne D. Joseph & Robert G. Ackman, *Capillary Column Gas Chromatographic Method for Analysis of Encapsulated Fish Oils and Fish Oil Ethyl Esters: Collaborative Study*, 75 J. of AOAC Int'l 488 (1992); Terje Tande, Harald Breivik & Terje Aasoldsen, *Validation of a Method for Gas Chromatographic Analysis of Eicosapentaenoic Acid and Docosahexaenoic Acid as Active Ingredients in Medicinal Products*, 69 J. AOCS 1124 (1992); Jeanne D. Joseph & Glorinda T. Seaborn, Chapter 3: *The Analysis of Marine Fatty Acids in Fish Oils in Nutrition* 40 (Maurice E. Stansby ed.).

Community for medicinal preparations. Area percentages are always greater than weight percentages (see footnote) and, as Dr. Breivik's research demonstrates (see his Tables 1-4), do not accurately reflect the actual compositions of the products. The Cornieri patent doesn't address this issue of quantitation at all, states only that GLC was used to monitor the process, and so I assume that they used the simplest procedure, i.e., area percent composition.

6) I further declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed by me to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of any patent that might issue on the above-identified application.

Date: August 18, 1994

  
Jeanne D. Joseph

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